

Fibrosis Assessed by Non-Invasive Tests is Similar to Liver Biopsy for Predicting Clinical Outcomes: A TARGET-NASH Study

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INTRODUCTION

- Liver biopsy is the standard for assessing fibrosis and diagnosing cirrhosis.
- Whether non-invasive tests (NITs) of fibrosis can predict outcomes such as decompensation events (DCC), incident ascites, variceal bleeding, hepatic encephalopathy), liver transplantation (LT), hepatocellular carcinoma (HCC), or death, as well as liver biopsy is unknown.

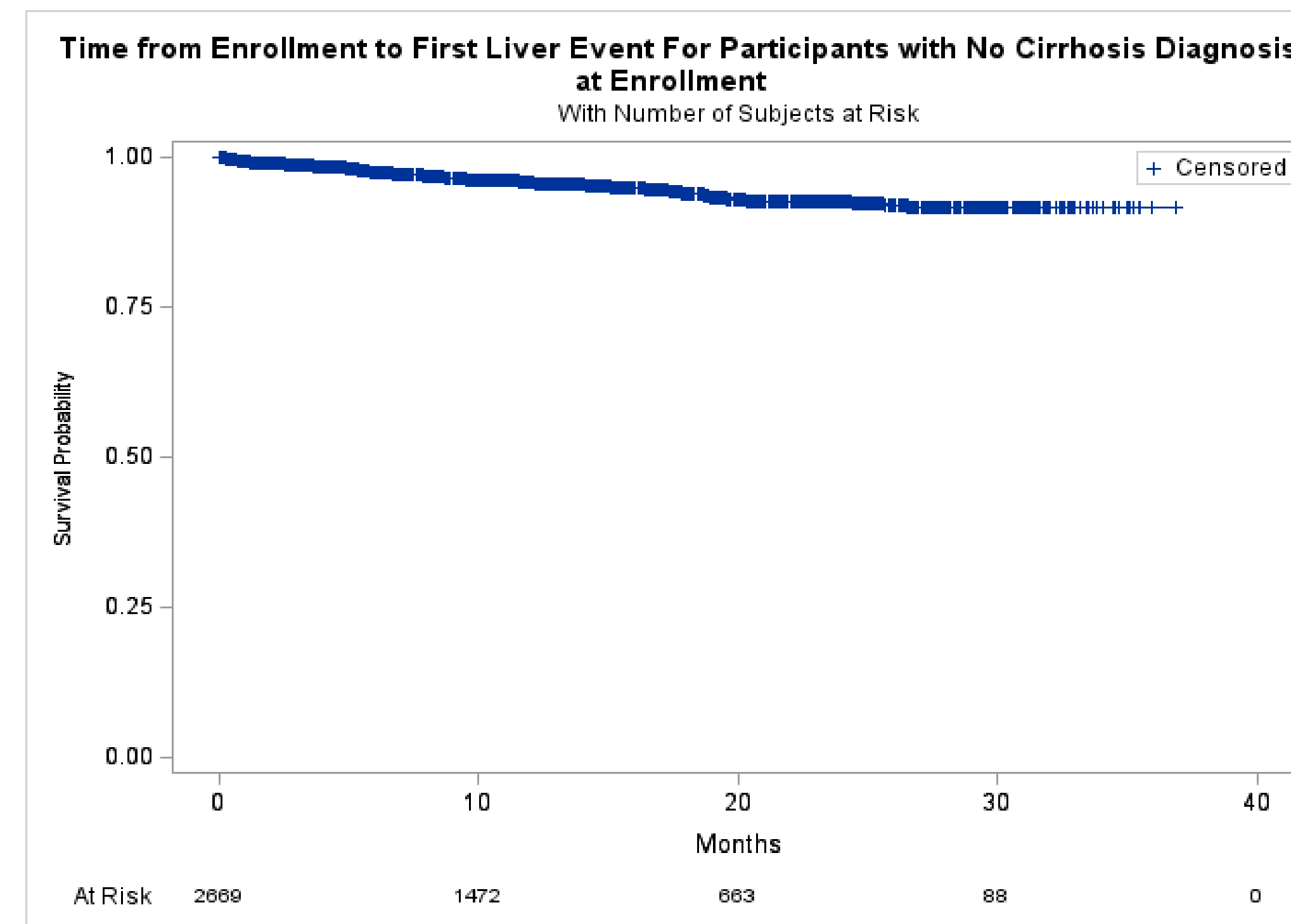
OBJECTIVE

- This study sought to compare compensated cirrhosis diagnosed clinically or by NITs to liver biopsy for predicting the clinical outcomes of DCC, HCC, LT and death.

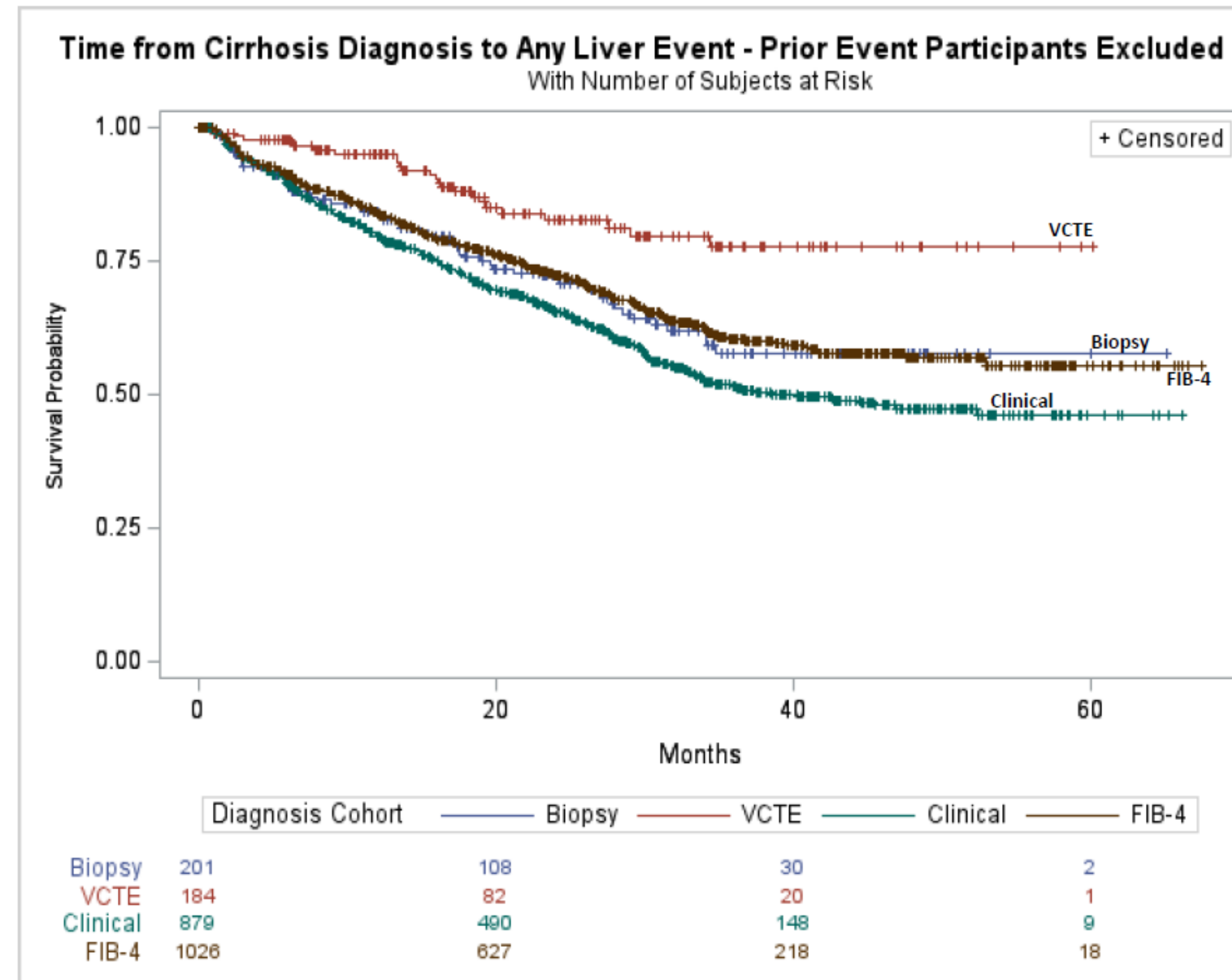
METHODS

- TARGET-NASH is a longitudinal cohort of patients with NAFLD receiving care in usual clinical practice in the US¹.
- Patients diagnosed with cirrhosis by liver biopsy, NIT (FIB-4 ≥ 2.67), vibration controlled transient elastography (VCTE ≥ 16 kPa), or a clinical algorithm were included.
- Outcomes were DCC (ascites, encephalopathy, variceal bleeding), HCC, LT, and death.
- Patients with events prior to or within 30 days of a diagnosis of cirrhosis were excluded.
- Patients without cirrhosis were analyzed for the same outcomes as a sensitivity analysis.
- Time to first event analyses were performed to assess the performance of NITs and clinical diagnoses compared to liver biopsy.
- Hazard ratios (HR) were calculated to see if there was a different probability of events based on method of diagnosis.

Figure 1. Time to Event for Patients Without Cirrhosis (A) and With Cirrhosis (B)



A



B

RESULTS

- Of the 4,102 adult patients from TARGET-NASH, 1,388 had at least one diagnostic criteria for cirrhosis: biopsy (n=239), FIB-4 (n=1286), VCTE (n=199) or clinical criteria (n=1152).
- In participants with cirrhosis there were 401 (28.9%) with *de novo* DCC, 27 (1.9%) with incident HCC, 32 (2.3%) with LT and 72 deaths (5.2%). 2,714 patients without a diagnosis of cirrhosis had 112 events in total.
- The HR for patients without cirrhosis by any diagnostic criteria for first liver event was 0.21 (0.17,0.26) compared to patients with cirrhosis.
- Unadjusted HRs compared time to first liver event for FIB-4 diagnosis vs biopsy diagnosis (0.95 (0.70,1.30)), VCTE diagnosis vs biopsy diagnosis (0.44 (0.27,0.73)) and clinical diagnosis vs biopsy diagnosis (1.27 (0.92,1.74)).
- Kaplan-Meier curves to first event are in Figure 1.

CONCLUSIONS

- **A diagnosis of advanced fibrosis/cirrhosis may be made by FIB-4 predicted clinical outcomes as well as biopsy.**
- **Cirrhosis diagnosed by VCTE liver stiffness ≥ 16 kPa may overestimate disease severity as events occurred at a lower rate.**
- **Patients diagnosed using clinical criteria may already have signs of portal hypertension and thus predictably experience clinical outcomes at a numerically higher rate albeit not statistically significantly greater than other means of diagnosis.**
- **Importantly, patients without a diagnosis of cirrhosis suffered few events over time.**

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¹ Barritt AS, Gitlin N, Klein S, Lok AS, Loomba R, Malahias L, Powell M, et al. Design and rationale for a real-world observational cohort of patients with nonalcoholic fatty liver disease: The TARGET-NASH study. *Contemp Clin Trials* 2017;61:33-38.